IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No.: 5963
Chernajovsky *et al.* #5	Art Unit: 1614
Appl. No. 09/756,283	Examiner: *To be assigned*
Filed: January 9, 2001	Atty. Docket: 0623.1000000/EKS/PAJ
For: **Latent Fusion Protein**	

Preliminary Amendment and Submission of Sequence Listing

Commissioner for Patents
Washington, D.C. 20231

Sir:

In advance of prosecution, Applicants submit the following Preliminary Amendment and Remarks. This Amendment is provided in the following format:

(A) A clean version of each replacement paragraph/section along with clear instructions for entry;

(B) Starting on a separate page, appropriate remarks. 37 C.F.R. § 1.115; and

(C) Starting on a separate page, a marked-up version entitled: "Version with Markings to Show Changes Made."

It is not believed that extensions of time or fees for net addition of claims are required beyond those that may otherwise be provided for in documents accompanying this paper. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 19-0036.

Amendments

In the Specification:

On page 37, please substitute the following Table 4 for the pending Table 4:

Plasmid	Antiviral activity (U/ml)
LAP-mIFNβ	0
PorcLAP-mIFNβ	256
mIFNβ-LAP	256

Please insert the Sequence Listing at the end of the application.

In the Claims:

Please substitute the following claim 3 for the pending claim 3:

3. (Once amended) The use as claimed in claim 1 wherein the proteolytic cleavage site is a matrix metalloproteinase (MMP) cleavage site.

Please substitute the following claim 4 for the pending claim 4:

4. (Once amended) The use as claimed in claim 1 wherein the pharmaceutically active is a growth factor, differentiation factor, cytokine, chemokine, trophic factor, cytokine inhibitor, cytokine receptor, free-radical scavenging enzyme, peptide mimetic, protease inhibitor, tissue inhibitor of metalloproteinase sub class, inhibitor of serine protease, chemotherapeutic agent or peptide nucleic acid sequence.

Please substitute the following claim 5 for the pending claim 5:

5. (Once amended) The use as claimed in claim 1 wherein the fusion protein is in association with latent TGFβ binding protein.

Please substitute the following claim 7 for the pending claim 7:

7. (Once amended) A nucleic acid construct as claimed in claim 6 wherein the first nucleic acid sequence encodes the protein INFβ.

Please substitute the following claim 8 for the pending claim 8:

8. (Once amended) A nucleic acid construct as claimed in claim 6 which is in the form of a vector.

Please substitute the following claim 9 for the pending claim 9:

9. (Once amended) A cell comprising a nucleic acid construct as claimed in claim 6.

Please substitute the following claim 10 for the pending claim 10:

10. (Once amended) A method of treatment of a patient comprising administering to said patient a therapeutically effective amount of a nucleic acid construct as claimed in claim 6.

Please substitute the following claim 12 for the pending claim 12:

12. (Once amended) A method of treatment as claimed in claim 10 wherein the treatment is gene therapy.

Please substitute the following claim 13 for the pending claim 13:

13. (Once amended) A nucleic acid construct as claimed in claim 6 for use in medicine.

Please substitute the following claim 14 for the pending claim 14:

14. (Once amended) Use of a nucleic acid construct as claimed in claim 6 in the manufacture of a medicament for the treatment of an inflammatory disorder.

Please substitute the following claim 15 for the pending claim 15:

15. (Once amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a nucleic acid construct as claimed in claim 6.

Please substitute the following claim 23 for the pending claim 23:

23. (Once amended) A kit comprising a nucleic acid construct as claimed in claim 6 and an administration vehicle.

Please add the following new claim:

24. (New) A kit comprising a fusion protein as claimed in claim 16, and an administration vehicle.

In the Abstract:

Please insert the following abstract after page 44 of the specification:

LATENT FUSION PROTEIN

ABSTRACT OF THE DISCLOSURE

This invention provides a nucleic acid construct comprising a first nucleic acid sequence encoding a pharmaceutically active agent and a second nucleotide sequence encoding a latency associated peptide, in which a nucleic acid sequence encoding a proteolytic cleavage site is provided between the first and second nucleic acid sequences. The invention further provides a fusion protein comprising a latency associated peptide and a proteolytic cleavage site wherein the fusion protein is associated with a pharmaceutically active agent. Also disclosed are processes for preparing the construct and fusion protein, methods of treatment using the construct and fusion protein and pharmaceutical compositions containing the construct and fusion protein.

Remarks

No new matter is added by way of this amendment. The specification has been amended to include an Abstract as required by 37 C.F.R. § 1.72(b), to insert the Sequence Listing and to correct an obvious typographical error. On page 37 in Table 4 of the specification, the word "LAP-mIFNβ" was mistakenly excluded. To correct this obvious editorial error, the word has been inserted by amendment. One skilled in the art would not only recognize the existence of the error at page 37, but also the appropriate correction from a reading of Example 3. The claims have been amended merely to reduce the number of multiple dependent claims and to correct an obvious typographical error. Support for claim 24 can be found, *inter alia*, in original claim 23.

In accordance with 37 C.F.R. § 1.821(f), the paper copy of the Sequence Listing and the computer readable copy of the Sequence Listing submitted herewith in the above-captioned application are the same. In accordance with 37 C.F.R. § 1.821(g), this submission includes no new matter.

It is believed that the application is now in condition for examination. Early notice to this effect is respectfully requested.

Respectfully submitted,

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Version with Markings to Show Changes Made

In the Specification:

On page 37, the following Table 4 replaced the pending Table 4:

Plasmid	Antiviral activity (U/ml)
LAP-mIFNβ [0]	0
PorcLAP-mIFNβ	256
mIFNβ-LAP	256

The Sequence Listing was added at the end of the application.

In the Claims:

Claims 3-5, 7-10, 12-15 and 23 were amended as follows:

3. (Once amended) The use as claimed in [any] claim 1 [or claim 2] wherein the proteolytic cleavage site is a matrix metalloproteinase (MMP) cleavage site.

4. (Once amended) The use as claimed in claim 1 [any one of the preceding claims] wherein the pharmaceutically active is a growth factor, differentiation factor, cytokine, chemokine, trophic factor, cytokine inhibitor, cytokine receptor, free-radical scavenging enzyme, peptide mimetic, protease inhibitor, tissue inhibitor of metalloproteinase sub class, inhibitor of serine protease, chemotherapeutic agent or peptide nucleic acid sequence.

5. (Once amended) The use as claimed in claim 1 [any one of the preceding claims] wherein the fusion protein is in association with latent TGFβ binding protein.

7. (Once amended) A nucleic acid construct as claimed in claim 6 wherein the first nucleic acid sequence encodes the protein INFβ.

8. (Once amended) A nucleic acid construct as claimed in claim 6 [or claim 7] which is in the form of a vector.

9. (Once amended) A cell comprising a nucleic acid construct as claimed in claim 6 [any one of claims 6 to 8].

10. (Once amended) A method of treatment of a patient comprising administering to said patient a therapeutically effective amount of a nucleic acid construct as claimed in claim 6 [any one of claims 6 to 8].

12. (Once amended) A method of treatment as claimed in claim 10 [or claim 11] wherein the treatment is gene therapy.

13. (Once amended) A nucleic acid construct as claimed in claim 6 [any one of claims 6 to 8] for use in medicine.

14. (Once amended) Use of a nucleic acid construct as claimed in claim 6 [any one of claims 6 to 8] in the manufacture of a medicament for the treatment of an inflammatory disorder.

15. (Once amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a nucleic acid construct as claimed in claim 6 [any one of claims 6 to 8].

23. (Once amended) A kit [of parts] comprising a nucleic acid construct as claimed in claim 6 [any one of claims 6 to 8, or a fusion protein as claimed in claim 16,] and an administration vehicle.

Claim 24 was added.

In the Abstract:

An abstract was added after page 44 of the specification.